

Lineage tracing with Axin2 reveals distinct developmental and adult populations of Wnt/beta-catenin-responsive neural stem cells.

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Public Summary:

This paper addresses the function of neural stem cells in the mammalian brain, and how these cells are generated and maintained. As the Wnt signaling pathway is crucial for development of the central nervous system, we examined the role of Wnt signaling during neural stem cell maintenance and differentiation. We were able to label neural stem cells using a recently developed mouse strain and thereby follow the developmental fate of Wnt-responsive cells in both the embryonic and postnatal mouse brain. From as early as embryonic day 8.5 onwards, we found neural stem cells being labeled in functionally restricted populations. Labeling in the postnatal brain demonstrated the persistence of long-lived, Wnt responsive stem cells in both of these sites. These results demonstrate the continued importance of Wnt signaling for neural stem and progenitor cell formation and function throughout developmental time and have implications for cancer from this tissue as well.

Scientific Abstract:

Since the discovery of neural stem cells in the mammalian brain, there has been significant interest in understanding their contribution to tissue homeostasis at both the cellular and molecular level. Wnt/beta-catenin signaling is crucial for development of the central nervous system and has been implicated in stem cell maintenance in multiple tissues. Based on this, we hypothesized that the Wnt pathway likely controls neural stem cell maintenance and differentiation along the entire developmental continuum. To test this, we performed lineage tracing experiments using the recently developed tamoxifen-inducible Cre at Axin2 mouse strain to follow the developmental fate of Wnt/beta-catenin-responsive cells in both the embryonic and postnatal mouse brain. From as early as embryonic day 8.5 onwards, Axin2⁺ cells can give rise to spatially and functionally restricted populations of adult neural stem cells in the subventricular zone. Similarly, progeny from Axin2⁺ cells labeled from E12.5 contribute to both the subventricular zone and the dentate gyrus of the hippocampus. Labeling in the postnatal brain, in turn, demonstrates the persistence of long-lived, Wnt/beta-catenin-responsive stem cells in both of these sites. These results demonstrate the continued importance of Wnt/beta-catenin signaling for neural stem and progenitor cell formation and function throughout developmental time.

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